

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-26 (Canceled).

Claim 27 (Previously Presented): A method of screening operating conditions of a coupling reaction of at least two functional groups, comprising:

i) reacting together at least two compounds:

a first compound of formula $E_1-X_1-G_1$ in which G_1 represents a first of said at least two functional groups, X_1 represents a covalent bond or a first spacer group, and E_1 represents the residue of a first molecule M_1 for which a first specific antibody AC_1 is available; and

a second compound of formula $E_2-X_2-G_2$ in which G_2 represents a second of said at least two functional groups, X_2 represents a covalent bond or a second spacer group, which is optionally identical to or different from X_1 , and E_2 represents either a residue of a second molecule M_2 that is different from M_1 and for which a second specific antibody AC_2 is available, or a group capable of forming at least one covalent bond with the antibody AC_1 in the presence of a coupling agent,

wherein said at least two compounds are reacted in a solution comprising a solvent under predetermined operating conditions comprising a candidate operating condition to obtain a reaction medium and in the reaction medium, to obtain a compound Z composed of the chain $E_1-X_1-G_1-G_2-X_2-E_2$, wherein G_1-G_2 represents the group of atoms resulting from the coupling of said at least two functional groups;

ii) determining the concentration of the obtained compound Z in the reaction medium at a predetermined reaction time t , by at least one immunoassay, said immunoassay comprising at least:

bringing the reaction medium obtained at reaction time t into contact with a solid phase on which the first antibody AC1 is immobilized so as to obtain the attachment of the compound Z to said solid phase by immunobinding between the antibody AC1 and the residue E₁ of the compound Z;

removing the reaction medium;

measuring the amount of compound Z attached to the solid phase; and

determining, on a standard range, the concentration of the obtained compound Z in the reaction medium at said time t, from the amount of compound Z thus measured; and

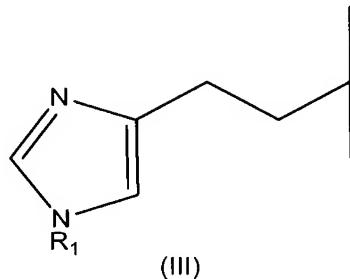
iii) evaluating the effects of the candidate operating condition(s) on said coupling reaction by the concentration of compound Z thus determined.

Claim 28 (Previously Presented): The method according to Claim 27, wherein the coupling reaction is selected from the group consisting of esterification reactions, amidation reactions, aldolization and nitroaldolization reactions, the Heck reaction, the Baylis-Hillman reaction, the Michael reaction, metathesis reactions, the Diels-Alder reaction, the Sonogashira reaction, the Suzuki reaction, the Kumada reaction, the Stille reaction, the Hiyama reaction, the Liebeskind-Srogl reaction, the Mannich reaction, the Hantzsch reaction, the reaction comprising coupling an α -ketoaldehyde with a carboxylic acid and an isonitrile to obtain an oxazole, the Ugi reaction, and variants thereof.

Claim 29 (Previously Presented): The method according to Claim 27, in which E₁ or E₂ represents the histamine residue.

Claim 30 (Canceled).

Claim 31 (Previously Presented): The method according to Claim 29, in which E₁ or E₂ is a compound of formula (III) below:



in which R₁ represents a hydrogen atom or a protective group.

Claim 32 (Canceled).

Claim 33 (Previously Presented): The method according to Claim 27, in which E₂ represents a group chosen from amine, carboxylic acid, aldehyde, thiol, phenol, alkenyl and azide groups, and photoactivatable groups.

Claim 34 (Previously Presented): The method according to Claim 33, in which E₂ represents an amine or thiol group.

Claim 35 (Previously Presented): The method according to Claim 27, in which said at least one immunoassay for the compound Z is a solid-phase assay.

Claim 36 (Canceled).

Claim 37 (Previously Presented): The method according to Claim 27, wherein E₂ is a group capable of forming at least one covalent bond with the first antibody AC₁, and the ii) comprises:

- a₂) bringing the reaction medium obtained at reaction time t into contact with a solid phase on which the first antibody AC₁ is immobilized, so as to obtain the attachment of the compound Z to the solid phase by immunobinding between the antibody AC₁ and the residue E₁ of the compound Z;
- b₂) reacting a coupling agent with the first antibody AC₁ immobilized on the solid phase and the group E₂ of the compound Z attached to the solid phase, so as to obtain the formation of one or more covalent bonds between the antibody AC₁ and the group E₂;
- c₂) denaturing the immunobond which exists between the first antibody AC₁ immobilized on the solid phase and the residue E₂ of the compound Z attached to the solid phase, so as to release the residue E₂ from the solid phase;
- d₂) bringing the solid phase into contact with a conjugate comprising the first antibody AC₁ coupled to a label, so as to obtain the attachment of the conjugate to the solid phase by immunobinding between the antibody AC₁ and the residue E₁ of the compound E₁-X-G₁-G₂-Y-E₂ thus released;
- e₂) measuring the amount of conjugate attached to the solid phase by the label coupled to the antibody AC₁; and
- f₂) determining, on a standard range, the concentration of compound Z in the reaction medium at said time t, from the amount of conjugate thus measured;

said ii) further comprising one or more operations comprising washing the solid phase, between a₂) and b₂), b₂) and c₂), c₂) and d₂), and between d₂) and e₂).

Claim 38 (Previously Presented): The method according to Claim 27, in which the first antibody AC₁ is a monoclonal antibody.

Claim 39 (Canceled).

Claim 40 (Previously Presented): The method according to Claim 27, in which the solid phase is the wall of a well of a microtitration plate onto which the first antibody AC₁ is adsorbed.

Claim 41 (Canceled).

Claim 42 (Previously Presented): The method according to Claim 27, which comprises an operation comprising dilution of the reaction medium between the i) and ii).

Claim 43 (Previously Presented): The method according to Claim 27, in which the yield of the coupling reaction is determined from the concentration of compound Z in the reaction medium.

Claim 44 (Previously Presented): The method according to Claim 27, in which the coupling reaction comprises coupling 2, 3 or 4 functional groups.

Claim 45 (Previously Presented): The method according to Claim 44, in which the coupling reaction comprises coupling two functional groups G₁ and G₂, and in which: the compounds of formulae E₁-X₁-G₁ and E₂-X₂-G₂ are reacted together so as to obtain, in the reaction medium, a compound Z of the formula E₁-X₁-G₁-G₂-X₂-E₂ wherein the

G_1 - G_2 represents the group of atoms resulting from the coupling between said functional groups G_1 and G_2 ; and

the concentration of compound Z in the reaction medium is determined by one immunoassay.

Claim 46 (Canceled).

Claim 47 (Canceled).

Claim 48 (Previously Presented): The method according to Claim 27, in which the candidate operating condition(s) is(are) selected from the group consisting of solvents, catalysts, temperature levels, pressure levels, the use of ultrasound, concentrations, stoichiometric ratios, reaction times and combinations thereof.

Claim 49 (Previously Presented): The method according to Claim 27, in which the candidate operating condition(s) is(are) catalysts.

Claim 50 (Currently Amended): A kit for carrying out a method of screening the operating conditions of a coupling reaction of at least two functional groups, comprising suitable amounts:

of at least two compounds comprising:

a first compound of formula $E_1-X_1-G_1$ in which G_1 represents a first of said at least two functional groups, X_1 represents a covalent bond or a first spacer group and E_1 represents the residue of a first molecule M_1 ; and

a second compound of formula $E_2-X_2-G_2$ in which G_2 represents a second of said at least two functional groups, X_2 represents a covalent bond or a second spacer group, which is optionally identical to or different from X_1 , and E_2 represents the residue of a second molecule M_2 which is different from M_1 ;

of at least two antibodies comprising:

a first antibody AC_1 specific for the first molecule M_1 , the antibody AC_1 being optionally attached to a plurality of solid phases; and

a second antibody AC_2 specific for the second molecule M_2 , the antibody AC_2 being coupled to a label;

of a compound Z comprising the chain $E_1-X_1-G_1-G_2-X_2-E_2$, wherein the G_1-G_2 represents the group of atoms resulting from the coupling of said at least two functional groups; and, optionally:

of a reagent for visualizing the label;

~~of an agent for denaturing an immunobond which exists between the antibody AC_1 immobilized on the solid phase and the residue E_1 of the compound Z attached to said solid phase, so as to release the residue from said solid phase; and~~

of suitably chosen buffers.

Claim 51 (Previously Presented): A kit for carrying out a method of screening the operating conditions of a coupling reaction of at least two functional groups, comprising suitable amounts:

of at least two compounds comprising:

a first compound of formula $E_1-X_1-G_1$ in which G_1 represents a first of said at least two functional groups, X_1 represents a covalent bond or a first spacer group and E_1 represents the residue of a first molecule M_1 ; and

a second compound of formula $E_2-X_2-G_2$ in which G_2 represents a second of said at least two functional groups, X_2 represents a covalent bond or a second spacer group, that may be identical to or different from X_1 , and E_2 represents a group capable of forming one or more covalent bonds with an antibody specific for the molecule M_1 in the presence of a coupling agent;

of at least one antibody, this antibody being said antibody specific for the molecule M_1 ;

of a conjugate comprising said antibody specific for the molecule M_1 coupled to a label;

of a compound Z comprising the chain $E_1-X_1-G_1-G_2-X_2-E_2$, wherein G_1-G_2 represents a group of atoms resulting from the coupling of said at least two functional groups; and optionally

of at least one of a reagent for visualizing the label, a coupling agent, a reagent capable of denaturing an immunobond which exists between an antibody immobilized on a solid phase and a residue of the compound Z attached to said solid phase, so as to release the residue from said solid phase, and suitably chosen buffers.

Claim 52 (Previously Presented): A method for the screening of catalysts in a coupling reaction between two functional groups, comprising the screening method according to Claim 27.

Claim 53 (Canceled).

Claim 54 (Canceled).

Claim 55 (Previously Presented): The method according to Claim 27, wherein said immunoassay comprising at least:

bringing the reaction medium obtained at reaction time t into contact with a solid phase on which the first antibody AC1 is immobilized so as to obtain the attachment of the compound Z to said solid phase by immunobinding between the antibody AC1 and the residue E₁ of the compound Z;

reacting a coupling agent with the antibody AC1 immobilized on the solid phase and the group E2 of the compound Z attached to said solid phase, to achieve one or more covalent bonds between the antibody AC1 and the group E2;

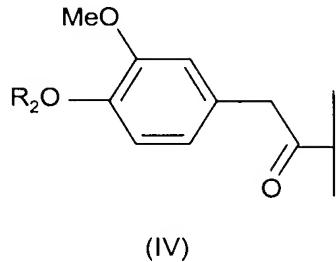
denaturing the immunobond which exists between the antibody AC1 immobilized on the solid phase and the residue E₁ of the compound Z attached to said solid phase, so as to release the residue from said solid phase;

removing the reaction medium;

measuring the amount of compound Z attached to the solid phase; and determining, on a standard range, the concentration of the obtained compound Z in the reaction medium at said time t, from the amount of compound Z thus measured.

Claim 56 (New): The method according to Claim 27, wherein E₁ or E₂ represents the homovanillic acid residue.

Claim 57 (New): The method according to Claim 31, wherein E₁ or E₂ corresponds to formula (IV) below:



wherein R₂ represents a hydrogen atom or a protective group.

Claim 58 (New): The method according to Claim 27, wherein, since E₂ corresponds to the residue of a molecule M₂, ii) comprises:

a₁) bringing the reaction medium obtained at reaction time t into contact with a solid phase on which the first antibody AC₁ is immobilized, so as to obtain the attachment of the compound Z on this solid phase by immunobinding between this antibody and the residue E₁, of this compound;

b₁) bringing the solid phase into contact with a conjugate comprising the second antibody AC₂ coupled to a label, so as to obtain the attachment of this conjugate to this solid phase by immunobinding between the second antibody AC₂ and the residue E₂ of the compound Z attached to said solid phase;

c₁) measuring the amount of conjugate attached to the solid phase by means of the label coupled to the antibody AC₂; and

d₁) determining, on a standard range, the concentration of the compound Z in the reaction medium at said time t , from the amount of conjugate thus measured;
said ii) also comprising one or more operations consisting in washing the solid phase, between a₁) and b₁), and between b₁) and c₁).

Claim 59 (New): The method according to Claim 27, wherein the second antibody AC₂ is a monoclonal antibody.

Claim 60 (New): The method according to Claim 36, wherein the label is an enzyme.

Claim 61 (New): The method according to Claim 36, wherein the label is acetylcholine esterase.